

REMARKS

Claims 12 and 13 have been canceled without prejudice. Claims 1, 4, 10, and 33 have been amended for greater clarity. New claims 34 and 35 have been added. Support for the claim amendments and new claims 34-35 can be found throughout the specification and in the original claims (e.g., claims 10, 12, and 13). No new matter has been introduced and no new issues have been raised.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Claim Rejections under 35 USC § 112, First Paragraph

With respect to the written description rejection, the Examiner asserts that "[i]t is not clear if the written description is sufficiently repeatable to avoid the need of for a deposit. Further, it is unclear if the starting materials were readily available to the public at the time of invention." Office Action, page 2, lines 14-16.

As the Examiner suggested, Applicants enclose herewith a declaration from the assignee of the application that the deposited material has been made at and accepted by the International Depositary Authority on August 27, 2002 under the Budapest Treaty on the international Recognition of the Deposit of Microorganisms for the purpose of Patent Procedure (e.g., see 961 OG 21, 1977), that the deposited material has been accorded a specific accession number: NM02/31074, and that all restriction on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent. A copy of the Deposit Receipt issued by the International Depositary Authority was submitted to the Examiner along with the Response filed on January 7, 2008.

Applicants believe that the enclosed declaration has obviate the rejection. Reconsideration and withdrawal of the rejection are respectfully requested.

Claim Rejections under 35 USC § 112, Second Paragraph

Claims 1, 4-15, and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. To expedite prosecution, Applicants have amended certain claims. Such amendments are not made in acquiescence of the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope.

a. Applicants contend that the recitation "a loss of growth of no more than log 3" in claim 1 is clear to one of skill in the art. Nevertheless, to expedite prosecution, Applicants have removed such recitation from claim 1 without prejudice, rendering the rejection moot.

b. Applicants contend that the recitation "no greater than 25% per six month storage" in claim 1 is clear to one of skill in the art. Nevertheless, to expedite prosecution, Applicants have removed such recitation from claim 1 without prejudice, rendering the rejection moot.

c. Regarding the recitation of "component" in claim 4, Applicants submit that the term "component" is clear to one of skill in the art since it is defined as "a product of disruption of a whole cell" of the claimed bacteria strain. Indeed, the specification describes procedures for preparing such components (e.g., the paragraph spanning pages 3 and 4) and teaches such components (e.g., page 6, lines 25-27). Furthermore, the specification describes activities of cell surface extracts (e.g., page 14, lines 13-16) and describes inhibitory activities of exemplary components such as low and high molecular weight metabolites of the lactobacillus (e.g., page 17, lines 17-30). Nevertheless, solely to expedite prosecution, Applicants have amended claim 4 to recite "an organic component." Applicants submit that a skilled artisan would know the metes and bounds of the term "organic component" when used in the context of the claimed strain.

d. Regarding the recitation of "in the form of ... a food product" in claims 10 and 12-13, Applicants traverse the Examiner's assertion that "it is apparent that the composition [in claim 10] is a food product" for the reasons already made of records. Nevertheless, solely for greater clarification, Applicants have amended claim 10 to remove the recitation of "dietary supplement or food product," and have cancelled claims 12 and 13 without prejudice, rendering the rejection moot.

Applicants have added new claim 34 which recites a food product comprising a *Lactobacillus fermentum* variant according to claim 1. New claim 35 depends from claim 34 and specifies that said food product is a dairy or dairy-based food product. Support for new claims 34-35 can be found throughout the specification and in the original claims (e.g., claims 10, 12, and 13). Applicants submit that new claims 34 and 35 are clear and definite to one of skill in the art.

In view of the above amendments and remarks, the Examiner is respectfully requested to reconsider and withdraw all rejections under 35 U.S.C. § 112, second paragraph.

Claim Rejections under 35 U.S.C. § 102(b) or § 103(a)

Claims 1, 4-5, 8-10, 12, and 14 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by, or in the alternative, under 35 USC 103(a) as allegedly obvious over Heinemann et al. (FEMS Microbiology Letters, 2000, vol. 190). Applicants traverse these rejections.

The standard for anticipating a claim is clearly outlined in MPEP 2131, and this standard is further supported by the Courts. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1978).

Applicants contend that Heinemann et al. fail to satisfy this criteria for anticipating the present invention. Although Heinemann et al. describe a strain of *Lactobacillus fermentum* RC-14, Heinemann et al. do **not** explicitly teach a biologically pure culture of a *Lactobacillus fermentum* variant VRI 003 (accession no. NM02/31074) comprising the characteristics as described in the application. In fact, the RC-14 strain is no longer considered to be a *Lactobacillus fermentum* according to the revision of the taxonomy – the RC-14 strain is now characterized as *Lactobacillus reuteri* (see the two articles listed on the enclosed SB/08 Form: Reid and Bruce, World J. Urol., 2006, 24, 28-32; and Reid and Hammond, Can Fam Physician. 2005 November 10; 51(11): 1487-1493). For example, the Reid and Bruce article teaches, on page 29, 2nd column, last paragraph, that "[s]tudies using vaginally administered *L. rhamnosus* GR-1 in combination with either *L. reuteri* (formerly *fermentum*) B54 or RC 14 have shown that vaginal colonisation can be achieved

..." (emphasis added). The Reid and Hammond article teaches, on page 1490, 2nd column, last paragraph before Figure 1, that "[t]here is level I evidence of the effectiveness of *L rhamnosus* GR-1 and *Lactobacillus reuteri* (formerly *fermentum*) B-54 and RC-14 in restoring vaginal *lactobacilli* and reducing infections" (emphasis added).

The Examiner asserts that "even if the claimed microorganism is not identical to the referenced microorganism with regard to some unidentified characteristics, the difference between that which is disclosed and that which is claimed are considered to be so slight that the referenced microorganism is **likely to inherently** possess the same characteristics of the claimed microorganism particularly in view of the similar characteristics which they have been shown to share. Thus the claimed strain would have been obvious to those skilled in the art within the meaning of USC 103." (Office Action, page 6, first paragraph, emphasis added).

The Examiner appears to allege that the reference inherently teaches the instant invention. Applicants respectfully disagree. According to MPEP 2112, "[T]he fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic." Further, one court observed that an inherency rejection is valid only if the result "must" occur. See *Continental Can Company v. Monsanto*, 984 F.2d 1264 (Fed. Cir. 1991). This states, "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient." *Id.* at 1269.

The case law is clear: inherent anticipation requires more than mere accidental or unrecognized achievement of the same result. Here, the strain of *Lactobacillus fermentum* RC-14 in Heinemann et al. is now characterized as *Lactobacillus reuteri*, rather than *Lactobacillus fermentum*. As such, one of skill in the art would know that this cited prior art strain does not necessarily have all the characteristics of the claimed strain.

In addition, Heinemann et al. describe the RC-14 strain as "an isolate from the urogenital tract of a healthy woman" (see page 177). In contrast, the presently claimed strain was isolated from the gastrointestinal tract of a healthy human individual. Applicants disagree with the

Examiner's assertion that "[t]he site of isolation is not indicative of the properties of the strains compared." It is well known that the source of a *Lactobacilli* strain is key in determining its characteristics. The population of *Lactobacilli* in the gastrointestinal tract is known to be influenced by several factors, such as diet, antibiotics and stress. For example, Reuter explains in an article (Reuter, Gerhard. Current Issues in Intestinal Microbiology 2001. 2(2) 43):

The gastrointestinal microflora is a very complex community. Within the gastrointestinal tract, different habitats have to be recognized, e.g. mouth, stomach, small intestine (especially lower jejunum and ileum), large intestine (caecum, colon) and rectum. Normally, near stability exists in these habitats. The balance is influenced primarily by the host's individuality....Each person will have an individually fixed microflora as far as qualitative structure and the quantities of lactobacilli and bifidobacteria are concerned (Refs). This fact is of great interest, as more than 400 species within the intestinal microflora can be identified and may attain population levels nearly as high as 10^{12} /g in the colon (Refs).

Reuter continues by stating:

Some reports in the literature ignore the differences of the intestinal microflora between infants on one hand, and adults and elderly people on the other. In these age groups, lactobacilli and bifidobacterial populations are substantially different in structure and quantities. While lactobacilli are changing only quantitatively, probably after they have randomly colonized immediately after birth, the development of the bifidobacteria microflora is influenced by nutritional factors also (e.g. in-breast fed or formula-fed infants) or by the age of an individual.

In view of the above, even if Heinemann's strain **may** share a characteristic with the claimed strain (e.g., the ability to inhibit pathogens), a skilled artisan would know that there is no guarantee that the claimed strain will be taught in Heinemann et al. in view of the revised characterization as *Lactobacillus reuteri* (rather than *Lactobacillus fermentum*) and the distinct source of this prior art strain. Accordingly, Heinemann et al. fail to meet the limitations of independent claim 1, and thus fail to anticipate the claimed subject matter. For the same reasons, all claims that depend from claim 1 are not anticipated by Heinemann et al.

Applicants further submit that none of the other cited references bridge the gap between Heinemann et al. and the claimed invention (e.g., a *Lactobacillus fermentum* variant VRI 003 (accession no. NM02/31074) comprising the characteristics as described in the specification). Accordingly, all claims are not rendered obvious by Heinemann et al.

Claim Rejections under 35 U.S.C. § 102(b) or § 103(a)

Claims 1, 4-5, 8-10, 12-15, and 33 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by, or in the alternative, under 35 USC 103(a) as allegedly obvious over Mikelsaar et al. Applicants traverse these rejections.

Applicants contend that Mikelsaar et al. fail to satisfy this criteria for anticipating the present invention. Mikelsaar et al. describe a strain of *Lactobacillus fermentum* ME-3 which was isolated from a faecal sample of a healthy child (see page 4). Mikelsaar et al. state that the strain *L. fermentum* ME-3 is resistant to several antibiotics, namely metronidazole, ofloxacin, aztreonam, cefoxitin, and TMP-SMX (see pages 7-8). By contrast, the antibiotic resistance profile of the claimed VRI 003 deposit strain clearly differs from that of the strain cited in Mikelsaar et al. as shown in **Exhibit E** (submitted in the previous response).

The Examiner asserts that "[t]he Appendix E has been fully considered. However, the alleged differences [in] antibiotic resistance are not borne out by the data in this Appendix, since the antibiotics recited in Mikelsaar et al. are not mentioned with any specificity in the document proffered" (Office Action, page 8, last paragraph).

Applicants respectfully disagree. The Exhibit E describes the results comparing the antibiotic susceptibility pattern of the claimed VRI 003 strain to that of other strains of *Lactobacillus fermentum*. In this study, the minimal inhibitory concentration (MIC) of 12 antibiotics was investigated for 60 different *L. fermentum* isolates from commercial samples. The antibiotic testing regime applied in the study was based on the recommendations of the European Food and Safety Authority (EFSA) for the assessment of bacteria for resistance to antibiotics of human and veterinary importance (The EFSA Journal.223:1-12.2005). The antibiotic resistance profile of the claimed VRI 003 strain shows MIC values above the breakpoint values recommended for some antibiotics by EFSA. One of skill in the art would appreciate that the antibiotic resistance profile of the claimed VRI 003 strain differs to that cited in Mikelsaar et al.

In view of the above, even if Mikelsaar's strain **may** share a characteristic with the claimed strain (e.g., the ability to inhibit pathogens), a skilled artisan would know that there is no guarantee

that the claimed strain will be taught in Mikelsaar et al. due to the distinct antibiotics resistance profile of these strains. Accordingly, Mikelsaar et al. fail to meet the limitations of independent claim 1, and thus fail to anticipate the claimed subject matter. For the same reasons, all claims that depend from claim 1 are not anticipated by Mikelsaar et al.

Applicants further submit that none of the other cited references bridge the gap between Mikelsaar et al. and the claimed invention (e.g., a *Lactobacillus fermentum* variant VRI 003 (accession no. NM02/31074) comprising the characteristics as described in the specification). Accordingly, all claims are not rendered obvious by Mikelsaar et al.

In sum, the requirements for establishing a prima facie case of obviousness have not been satisfied. Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

Claim Rejections under 35 U.S.C. § 102(b) or § 103(a)

Claims 1, 4-5, 8-10, 12, 14, and 33 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by, or in the alternative, under 35 USC 103(a) as allegedly obvious over Blomberg et al. (Applied and Environmental Microbiology, 1993, vol. 59(1), pages 34-39). Applicants traverse these rejections.

Applicants contend that Blomberg et al. fail to satisfy this criteria for anticipating the present invention. Although Blomberg et al. describe a strain of *Lactobacillus fermentum* of porcine origin, Blomberg et al. do not explicitly teach a biologically pure culture of a *Lactobacillus fermentum* variant VRI 003 (accession no. NM02/31074) comprising the characteristics as described in the specification.

Applicants further submit that Blomberg et al. do not inherently teach the claimed strain of *Lactobacillus fermentum*. Blomberg et al. describe several strains of *Lactobacillus* of porcine origin, in particular, a *Lactobacillus fermentum* 104R isolated from porcine gastric squamous epithelium (see page 34). The particular strain described in Blomberg et al. was isolated from porcine gastric squamous epithelium. By contrast, the claimed VRI 003 was an isolate derived from

a human faecal sample. One of skill in the art would know that there is no guarantee that the claimed strain will be taught in Blomberg et al., given the distinct sources of these strains.

In view of the above, even if Blomberg's strain **may** share a characteristic with the claimed strain (e.g., the antimicrobial effect), a skilled artisan would know that there is no guarantee that the claimed strain will be taught in Blomberg et al. due to the distinct sources of these strains. Furthermore, it would not necessarily be obvious, contrary to the Examiner's assertion, that Blomberg's strain would be suitable for inclusion in a "food product", in view of the fact that the strain was isolated from a pig. Accordingly, Blomberg et al. fail to meet the limitations of independent claim 1, and thus fail to anticipate the claimed subject matter. For the same reasons, all claims that depend from claim 1 are not anticipated by Blomberg et al.

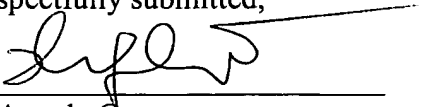
Applicants further submit that none of the other cited references bridge the gap between Blomberg et al. and the claimed invention (e.g., a *Lactobacillus fermentum* variant VRI 003 (accession no. NM02/31074) comprising the characteristics as described in the specification). Accordingly, all claims are not rendered obvious by Blomberg et al.

CONCLUSION

In view of the above amendment, applicant believes the pending application is in condition for allowance. If an additional fee is due, please charge our Deposit Account No. 18-1945, under Order No. **BSWV-P01-008** from which the undersigned is authorized to draw. In view of the above amendment, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

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